GenCore version 5.1.3 Compared Ltd  $(\gamma)$  1997 (2008)

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11055,609 Million cell updates/sec
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Pred. No. is the number of results predicted by chance to have a score greater than or equal to the score of the result being printed, and is derived by analysis of the total score distribution.

		æ				
Result		Query				
No.	Score	Match	Match bength DB	퍐	- 10	Description
_ :	26	100.0	į	24	ABI.57124	Cattle growth horm
2	55	100.0		13	ABL57128	Cattle growth horm
w	25	100.0		24	ABL57127	Cattle growth horm
4	25	100.0		12	ABL57126	Cattle growth horm
a 5	18.2	70.0		i)	AAS00247	Bcl-X1-DTR apoptos
c 6	18.2	70.0		.1 <b>8</b>	AAV05129	DNA cocoding dipth
c 7	18.2	70.0	1704	22	AAS00248	Bad-DTTR apoptosis
c 8	18.2	70 O		.n.	AA0=4340	Dightheria toxio (
c 9	18.2	70 0		1.5	AAQ54338	Diphtheria toxin d

r r x

Obtaining head of beef cattle with genetic predisposition for altered carcass weight, by assaying genetic material from head for polymorphism

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## ALIGNMENTS

12 X	PI	XX A	X Ŧ	YY PF	X PD	X P S	SO	XXX	X F	<b>X</b> 33	<b>( )</b>	RESULT 1 ABL57124 ID ABL
WF1; 2002-417707/45.	Lucy MC, Lubahn DB, Keisler DH, Shibuya H, Johnson GS, Herring WO; Hale CS;	(UMOR ) UNIV MISSOURI.	20-JUL-2000; Z000CA-2312269.	29-JUL-2000; 10000A-1312269.	20-JAN-2002.	CA2312269-A1.	Bos taurus.	Cattle, beef, breeding, growth hormone, somatotropin, receptor; midrosatellite, marker-assisted selection; PCR; primer; ss.	Cattle growth business receptor gene IS repeat 5' FOR primer.	05-A05 2002 (first entr/)	ABL57124;	LT 1 7124 ABL57124 standard: DNA; 26 BP.

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RESSULT 2
ARBL52128
TO ARBL52128
AC ARL5
AC AR
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Best Local .
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   05 - AUG - 2002
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    Sequence 26 BP; 4 A; 6 C; 6 G; 10 T; 0 other;
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            compared with cattle having tewer than 12 copies of the TG dinucleotide repeat. Use of this marker and other genetic markers in linkage disequilibrium with the locus allows implementation of
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         The present sequence is a primer that corresponds to nucleotides located 5' to a polymorphic G repeat microsatellite located 90 bp upstream from a major transcription start site in the bovine growth hormone receptor gene (see AH.57124). The "G-repeat microsatellite can be used as a genetic marker that correlates with cattle growth cattle having at least 12, and preferably 16-20, copies of the "G dinucleotide repeat marker show increased carcass or weaning weight
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               linked to promoter PL of exon 1A of bovine growth hormone receptor gene
                                          20 JUL 2000; 2000CA-2312269
                                                                                     20 JAN-2002.
                                                                                                                                                                                                                                                                                              variation
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                                                                                                                                                                                                                                                                                                                                                                variation
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100.0%; Prod. No. 0.023;
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     RESULT 3
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          Matches
                                                             exon
                                                                                                                                                                                                                                                                                                                                   microsatellite, marker assisted selection, ds
                                                                                                                                                                                                                                                                                                                                                         Cattle; beef; breeding; growth hormone; somatotropin;
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Lucy MC,
Haie CS;
Obtaining head of beef cattle with genetic predisposition for altered catcass weight, by assaying genetic material from head for polymorphism linked to promoter P1 of exon 1A of bovine growth hormone receptor gene
                                                                                                                                                                                                                                                                                                  (UMOR ) UNIV MISSOURI
                                                                                                                                     WPI; 2002-417707/45
                                                                                                                                                                                                                                 Lubahn DB, Keisler DH, Shibuya H,
                                                                                                                                                                                                                                 Johnson GS,
                                                                                                                                                                                                                                 Herring WO;
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Example 2; Fig 3; 51pp; English.

with the locus allows implementation.

with the locus allows implementation.

schemes for improvement of cattle performance. Other general markers may include polymorphisms such as the G/A polymorphic entries in contains a life in example. The A allele (found in indicine cattle) contains a Draf restriction site that is not present in the G allele (found in taurine cattle). This difference can be used in a PCR/RCLP in taurine cattle). This difference can be used in a PCR/RCLP in taurine cattle). This difference can be used in a PCR/RCLP in taurine cattle). in taurine cattle). This difference can be used in a PCR/RFLP assay to distinguish the respective aircies. The 2 P/C upstream polymorphic sites could similarly be used. Marker assisted selection with the genetic markers avoids the costry phenotypic testing associated with traditional breeding schemes. and carcass weight of cattle. Cattle having at least 12, and preferably 16-20, copies of the Te dinucleotide repeat marker show increased carcass or weaming weight compared with cattle having fewer than 12 copies of the TG dinucleotide repeat. Us start site in the gene is associated with average weaning weight this marker and other genetic markers in linkage disequilibrium with the locus allows implementation of selection and breeding buffine growth hofmute feeeptof gene. A polymorphic "G-repeat microsateilite located 90 bp upstream from a major transcription The present sequence is the promoter and exon IA region of the

Query Match Best Local S Sequence 522 BP; 124 A; 121 C; 136 G; 141 T; 0 other; 1 GIGGETAATGITTTCTGGTACCAGG 26 h 100.0%; Score 26; DS 24; Longth 522; Similarity 100.0%; Prod. No. 0.034; 26; Conservative 0, Mismatches 0, Indels 0,

0,

Cattle growth hormone receptor gene promoter and exon 1A region. 05-AUG-2902 ABL57127 standard; DNA; 540 207 GTGCTCTAATCTTTTCTGGTACCAGG 232 (first entry)

Bos taurus

variation sateilite primer\_bind /\*tag- c 362..540 /\*tag- b /mote- \*TG dimucleotide repeat microsatellite\* 293..318 febiace(lz,T) /\*tagcomplement (207..232) Location/Qualifiers /number- 1A 234. . 273 /\*tag=\_\_d C a

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RESULT 4
AHL57126
1D ABL5
XX
AC ABL5
XX
DT 05-4
XX
Catt
XX
Catt
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 В
                                                                                                                                                                                                                                                                                                                                                                 γ
                                                                                                                                                                                                                                                                                                                                                                                                                       Matches
                                                                                                                                                                                                                                                                                                                                                                                                                                                             Query Match
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          assay to distinguish the respective alleles. The 2 i/2 upstream polymorphic sites could similarly be used. Marker-assisted selection with the genetic markers avoids the costly phenotypic resting associated with traditional breeding schemes.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               with this marker and other genetic markers in linkage disequilibrium with the locus allows implementation of selection and breeding schemes for improvement of cattle performance. Other genetic markers may include polymorphisms such as the G/A polymorphic site in exon IA. The A allele (found in indicine cattle) contains a Drai restriction site that is not present in the G allele (found in taurine cattle). This difference can be used in a PCR/RFILD assay to distinguish the respective alleles. The 2 i/C upstream
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             bovine growth hormone receptor years. A polymorphic TG repeat microsatellite located 90 bp upstream from a major transcription start site in the gene is associated with average wearing weight and carcass weight of cattle. Cattle having at least 12, and preferably 16-20, copies of the TG dinucleotide repeat marker show increased carcass or wearing weight compared with cattle having fewer than 12 copies of the TG dinucleotide repeat. Use continuous processes the tensor of the TG dinucleotide repeat.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      CA2312269 A1
Cattle; beef; breeding; growth hormone; somatotropin; receptor;
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      Obtaining head of beef cattle with genetic predisposition for altered carcass weight, by assaying genetic material from head for polymorphism linked to promoter PI of exon IA of bovine growth hormone receptor gene
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       variation
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              Sequence 540 BP; 123 A; 123 C; 146 G; 148 T; 0 other;
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      Example 2: Fig 3; 51pp; English
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                WFI, 2002 417707,45
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    20-JUL-2000; 2000CA-2312269
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                                                Cattle growth
                                                                                                   05-AUC-2002
                                                                                                                                               ABL57126;
                                                                                                                                                                                                ABI.57126 standard; DNA;
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      The present sequence is the promoter and exon 1A region of the
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                Hale CS;
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       Lucy
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   (UMOR ) UNIV MISSOURI
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                                                                                                                                                                                                                                                                                                                   207 GEGGETANTETTTTTGGTACCAGG 232
                                                                                                                                                                                                                                                                                                                                                                                                                                         Local Similarity
                                                                                                                                                                                                                                                                                                                                                                 1 GTGCTCTAATCTTTTTCTGGTACCAGG 26
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     Lubahn DB,
                                                                                                                                                                                                                                                                                                                                                                                                                    Conservative
                                                                                              (first entry)
                                              hormone receptor gene promoter and exon 1A region
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             /*tag-
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       replace(94,T)
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/standard_name- "Single nucleotide polymorphism"
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 /standard_name-
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        /*Lag-
                                                                                                                                                                                                                                                                                                                                                                                                                                         100.0%; Score 26; DB 24; 166 6%; Pred No 6 634;
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     Keisler DH,
                                                                                                                                                                                                2869
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                                                                                                                                                                                                <del>В</del>
                                                                                                                                                                                                                                                                                                                                                                                                                    Mismatches
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               "Single nucleotide polymorphism"
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                Length 540;
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  Herring WO;
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  S S X P X S X B X
                                                                                                                                                                                                                                                                                         Вb
                                                                                                                                                                                             AAS00247
                                                                                                                                                                                                                    RESULT
                                                                                                                                                                                                                                                                                                                                                                                        Matches
                                                                                                                                                                                                                                                                                                                                                                                                                                 Query Match
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                Lovine growth hormore receptor gene. A polymorphic is-repeat microsatellite located 90 bp upstroam from a major transcription start site in the gene is associated with average wearing weight and carcass weight of cattle. Cattle having at least 12, and preferably 16-20, copies of the To dinvolentials repeat marker show increased carcass or wearing weight compared with cattle having fewer than 12 copies of the To dinvolection repeat. Use this marker and other genetic markers in linkage disequilibrium with the locus allows implementation of selection and breeding with the locus allows implementation of selection and breeding
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        microsatellite; marker-assisted selection; ds.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              schemes for improvement of cattle performance. Marker-assisted selection with the genetic markers avoids the costly phenotypic testing associated with traditional breeding schemes.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             Obtaining head of beef cattle with genetic predisposition for altered carcass weight, by assaying genetic material from head for polymorphism linked to promoter Pl of exon IA of bovine growth hormone receptor gene
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            Bcl-X1-DTR apoptosis-modifying fusion protein, DNA sequence
                                                                                                                                                                                                                                                                                         2580 GIGCICIAATCTTTTCTGGTACCAGG 2605
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     Sequence 2869 BP; 657 A; 640 C; 582 G; 990 T; 0 other;
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             Claim 3; Page 41-43; 51pp; English.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      WPI; 2002-417707/45.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       primer_bind
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                                                                  31-MAY-2001 (first entry)
                                                                                                                     AAS00247
                                                                                                                                                                    AAS00247 standard; DNA; 1236
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             The present sequence is the promoter and exon 1A region of the
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       Hale CS;
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                                                                                                                                                                                                                    J
                                                                                                                                                                                                                                                                                                                                                                                                               Local Similarity
                                                                                                                                                                                                                                                                                                                                     1 GTGCTCTAATCTTTTCTGGTACCAGG 26
                                                                                                                                                                                                                                                                                                                                                                                        26;
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            Lubahn DB,
                                                                                                                                                                                                                                                                                                                                                                                        Conservative
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               /*tag= c
2735..2869
/*tag= d
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2607..2646
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                                                                                                                                                                                                                                                                                                                                                                                                             100.0%;
100.0%;
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                                                                                                                                                                                                                                                                                                                                                                                                             Score 26; DB 24
Pred. No. 0.043;
                                                                                                                                                                                                                                                                                                                                                                                        Mismatches
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         Shibuya H,
                                                                                                                                                                                                                                                                                                                                                                                                                                 DB 24;
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Johnson GS,

Herring WO:

0;

0;

Caps

0;

Length 2869; Indels

Use of

Summado Bel XI DTR, apreptedia, cancer, apidal museular atruphy.

j.

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target cell and integrating into or crossing a cellular membrane of the target cell. The apoptosis modifying fusion protein comprises at least two domains: the DTR domain, which targets the fusion protein to the target cell and the BCL-XL domain, which modifies an apoptotic response of the target cell. The lusion protein is useful for modifying (inhibiting or enhancing) apoptosis in a target cell. Such as neuron, lymphocyte, caseer, scoplasm, macrophage, epithelial, stem, tamour of hyper-profiferative cell or an adjpocyte. It is also useful for reducing apoptosis in a subject after transient ischaemic neuronal injury, especially spiral cord injury conditions through inhibition or enhancement of apoptotic cellular response, including neurodegenerative disorders such as Alabelmer's discusse, lightington's discusse. Spiral mescular attaches and injury conditions to the spiral mescular attaches and an apoptotic cellular response, including neurodegenerative disorders such as Alabelmer's discusse. Unathopton's discusse. Spiral mescular
atrophy, stroke episodes and unregulated cell growth as in tumours and various cancers. The apoptosis modifying fusion protein can be delivered effectively throughout the body and targeted to selective tissue and
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     The sequence represents the coding sequence of BCL-XL-DTR apoptosis-a modifying fusion protein comprising human BCL-XL sequence fused via a start linker to diphtheria tookn receptor binding domain (DTR). The functional apoptosis-modifying fusion protein is capable of binding a
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           Novel fusion protein for modifying apoptosis in target cell and reducing apoptosis after transient ischaemic neuronal injury, has two domains which targets protein to a cell and modifies apoptotic response
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            Claim 5; Page 54:56; 65pp; English.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             misc_feature
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 Of C#11
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     P PSDB;
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   Youle RJ, Liu X, Collier RJ.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    (HARD) HARVARD COLLEGE.
(HSSH) US DEPT HEALTH & HUMAN SERVICES
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            15 AUG 2000; 2000WO-US22293
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           Chimer ic
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               16 AUG-1999;
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       Synthetic
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         Corynebacterium diptheriae
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               9908-0149220.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            Shoter
61. 37
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    /*tag- d
/mote- "linker DNA, linking Bel-XI to DTR"
778..1236
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             760.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                /*tag= b
/mote= "16x Histidine tag"
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             /note- "DTK, diphtheria toxin receptor binding domain"
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               /note- "Bel-X1 gene from codon 1-233"
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         /note- "DTR is diphtheria toxin receptor binding domain"
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           /*iaq-_a
/product-_"Bel-Xl-DTR lusion protein"
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              /*! aq-
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      Location/Qualifiers
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Matches 20;

Conservative

0; Mismatches

Indels

<u>.</u>;

Gaps

0

Longth 1608;

Query Match Best Local Similarity

70.0%; 87.0%;

Score 18.2; 58-18; Fred. No. 1.3e+02; sequence 1600 BP; 452 A; ມ94 c; 382 G; 440 T; 0 other;

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AAV05129/c
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       문
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           Query Match
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             Sequence 1236 BF, 317 A, 291 C, 343 C, 285
                                                                                   The present sequence encodes a diphtheria toxin. Regions of the present sequence can be utilised as broad range helper I cell epitopes in EMA plasmid hased vaccines against cholesteryl ester transfer proteins (CETPs). CETS mediate the transfer of cholesteryl esters from high density lipoprotein (NULL) and vice versa. An increased CETP activity produces an atherogenic lipoprotein profile and induces atheroscierosis. A DNA plasmid-based vaccine comprises sequences encoding at least one B cell epitope of CETP linked in frame with at least one sequent encoding a broad range helper T.cell epitope. The vaccines can be used to elevate
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       1188 GTGATCTACTGTTTTCTGGTACC 1166
                                  the ratio of circulating HDE to circulating LDE, VLDE or total cholesterol in a human. It can also be used for decreasing the level of endogenous CETF activity in a human. The vaccine can be used to produce
                                                                                                                                                                                                                                                                                                                         ENA plasmid based vaccine encodes CETP B cell and helper T cell epitope(s) - used for elevating high density lipoprotein levels, for treating cardiovascular disease
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         high density lipoprotein; HDL; very low density lipoprotein; VLDL; T cell epitope; antibody; DNA plasmid-based vaccine; broad range helper T cell epitope;
                 anti-CETP antibodies in vivo and for treating cardiovascular disease
                                                                                                                                                                                                                                                                                     Disclosure; Pages 40-42; 67pp; English.
                                                                                                                                                                                                                                                                                                                                                                                                   P-PSDH; AAW46448
                                                                                                                                                                                                                                                                                                                                                                                                                  WPI; 1997-549731/50
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      (TCEL-) T CELL
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            01-MAY-1995;
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             21-FEB-1997;
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               01-MAY-1997;
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   06-NOV-1997
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       W09741227-A1
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         Corynebacterium diphtheriae
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            treatment; cardiovascular disease; ss.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                Cholesteryl ester transfer protein, CETP; cholesteryl ester;
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      DNA encoding diptheria toxin
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        18-MAY-1998
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            AAV05129;
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              AAV05129 standard; cDNA; 1608
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        Local Similarity
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    1 GTGCTCTAATCTTTTCTGGTACC 23
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           Conscruative
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        (first entry)
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               97WO-US07294
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            96US-0640713
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      70.0%; Score 18.2; DB 22; 87.0%; Pred. No. 1.3e+02;
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           0
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           Mismatches
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               T; 0 other;
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             Length 1236;
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           Indels
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         Caps
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           0
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AAS00248/c
ID AAS002
    В
              target cell. The apoptosis modifying fusion protein comprises at least two domains: the DTR domain, which targets the fusion protein to the target cell and the Bcl XI domain, which targets the fusion protein to the (arget cell and the Bcl XI domain, which modifies an apprecial sequence (inhibiting or enhancing) apoptosis in a target cell, such as neuron, lymphocyte, cancer, neoplasm, macrophage, epithelial, stem, tumour or hyper-prollierative cell or an adipocyte. It is also useful for reducing apoptosis in a subject after translend ischamic neuronal injury, especially spinal cord injury. The fusion protein may be used to treat especially spinal cord injury conditions through inhibition or enhancement
                                                                                                                                                                                                                                                                                                                                                                               Novel fusion protein for modifying apoptosis in target cell and reducing apoptosis after transient ischaemic neuronal injury, has two domains which targets protein to a cell and modifies apoptotic response
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     Mouse: Bad-DTTR; apoptosis; cancer; spinal muscular atrophy; ds; diphtheria toxin receptor binding domain; DTTR; neoplasm; tumour; hyper-pro-iferation, Alzheimer's disease; neurodespectative disorder; transfent ischaemic neuronal injury; stroke; spinal cord injury;
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      1560
                                                                                                                                                                                                          functional apoptosis-modifying fusion protein is capable of binding a target cell and integrating into or crossing a cellular membrane of the
                                                                                                                                                                                                                                                modifying fusion protein comprising Bad gene sequence fused via
linker to diphtheria toxin translocation domain (DTTR). The
                                                                                                                                                                                                                                                                                                                         Claim 5; Page 57-59; 65pp; English
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    W0200112661-A2
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             Chimeric - Synthetic
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       Huntington's disease, diphtheria toxin translocation domain
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              31-MAY-2001
of apoptotic cellular response, including neurodegenerative disorders
                                                                                                                                                                                                                                                                                      The sequence represents the coding sequence of Bad-DTTR apoptosis-
                                                                                                                                                                                                                                                                                                                                                                                                                                                                 P-PSDB; AAU00220
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    16-AUG-1999;
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      15-AUG-2000; 2000WO-US22293
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   Bad-DTTR apoptosis-modifying fusion protein, DNA sequence
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        AAS00248 standard; DNA; 1704
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         (USSH ) US DEPT HEALTH & HUMAN SERVICES
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      CTCCTCTAATCTTTTCTGCTACC 23
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      GTGATCTACTGTTTTCTGGTACC 1538
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 2001-218343/22.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             BAPVARD COLLECT
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       Liu X, Collier RJ;
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 Mus sp
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 Corynebacterium diptheriae
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           (first entry)
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    9905-0149220
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            /note= "DTTR is diphtheria toxin translocation domain" 7..36
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       Location/Qualitiers
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          /*tag=
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              /product= "Bad-DTTR fusion protein"
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        /note= "10x histidine tag
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COGCCOCCEPTE SERVING S
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            Matches
gene (specifically the region encoding the DT A fragment) results in deletion of the codons for Vai 147 and active site residues Glu-148 and opt, deletion or substitution of other active residues. The resulting mateins are not toxic, making them useful in diphtheria vaccines. The risk of reversion to toxicity is much lower for the 147-148 double matants than for the prior art 148 single matant, while their immunogenicity is not impaired. The specification includes the wild-type DT coding sequence but does not include any matant sequences; the wild-type sequence was modified according to
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          such as Alzheimer's disease, Huntington's disease, spinal muscular atrophy, stroke episodes and unregulated evil growth as in tumours and various cancers. The appricasis modifying fusion protein can be delivered effectively throughout the body and targeted to selective tissue and
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   1656 GTGATCTACTGTTTTCTGGTACC 1634
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       DT; protein exotoxin: NAD-dependent ADP-ribosyltransferase; vaccine diphtheria toxold; deletion mutant; mutein; variant; double mutant;
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     AAQ54340 standard; DNA; 1921 BP
                                                                                                                                                                                                                                                                                                                                                                          Claim 4; ; 42pp; English.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                            New DNA encoding diphtheria toxin deletion mutants - with toxicity and low risk of reversion, and derived toxoids an
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  P-PSDB; AAR44892
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         17-MAY-1993;
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  Corynebacterium diphtheriae
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    Diphtheria toxin
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        Sequence 1704 BP; 470 A; 395 C; 444 G; 395 T; 0 other;
                                                                                                                                                                                                                                                                                                       Oligonucleotide directed mutagenesis of the wild-type diphtheria
                                                                                                                                                                                                                                                                                                                                                                                                                                            transformed cells, useful in vaccines
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     Collier PJ,
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    (HAPD ) HAPVARD COLLEGE
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          18-JUN-1992;
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            W09325210-A
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           reversion mutation; site-directed mutagenesis;
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            22-JUN-1994 (first entry)
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 œ
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              1994-007178/01.
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     Killeen K,
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          92US-0901712
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                /note- "single chain translation product is readily cleaved to form two subunits (A and B). line by a disulphide bond; wild-type codons 142
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         /product= deita-142_to_-148_diphtheria_toxin
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                312..1898
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         /*tag-
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               Location/Qualifiers
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                (delta-142 to 148) mutant coding sequence
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     70.0%;
87.0%;
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       to 148 have been deleted"
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     Mekalanos
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         0; Mismatches
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     Score 18.2; DB 22
Pred. No. 1.3e+02;
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        DB 22;
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        Length 1704;
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             vaccine;
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         0
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         Gaps
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          linked
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         0
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AAQS4338/c
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Best Local Similarity 87.0%;
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         Matches
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             the description in the claims to give AAQ54340.
                                                                                                                                 virilized. The (13) of (2001), 10 lower by the 147 148 doubte mutants than for the prior art 148 single mutant, while their immunogenicity is not impaired. The specification includes the wild type DT coding sequence but does not include any
                                                                                                                                                                                                                                                                          quie (specifically the region encoding the DF-A fragment) results in delection of the codons for Val-147 and active site residue. Glu 148 and opt, delection or substitution of other active residues. The resulting mutiples are not toxic multiply them result in diphtheria
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            1850 GTGATCTACTGTTTTCTGGTACC 1828
Sequence 1933 BP; 574 A; 359 C; 468 C; 533 T; 0 other;
                                                              mutant sequences; the wild type sequence was modified according to the description in the claims to give AAQ5438.
                                                                                                                                                                                                                                                                                                                                                                                                                       oligonucleotide directed mutagenesis of the wild-type diphtheria
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   Corynchasterium diphtheriae
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           Diphtheria toxin delta-142-147-148 mutant coding sequence
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       Sequence 1921 BP; 571 A; 357 C; 464 C; 530 T; 0 other;
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 Claim 3; ; 42pp; English
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       transformed cells, useful in vaccines
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     toxicity and low risk of reversion, and derived toxoids and
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   New DNA encoding diphtheria toxin deletion mutants - with no
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                P-PSDB; AAR44890
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     WP1; 1994-007178/01
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           (HARO ) HARVARD COLLEGE
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 18 JUN 1992;
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    17 MAY 1993;
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          23 DEC 1993.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  reversion mutation, site directed matagenesis, ds.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       diphtheria toxoid; deletion mutant; mutein; variant; double mutant;
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     OT; protein exotoxin; NAD dependent ADP-ribosyltransferase; vaccine;
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 22 JUN 1994 (first entry)
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           AAQ54338
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          AAQ54338 standard; DNA; 1933 BP
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          | LITERIAL | LITERIA | LIT
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     20;
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        Killeen K,
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 9208-0901712
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       93WO US04606.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        /product - delta 142 147 148_diphtheria_toxin
/mste- "simple chain translation product is readily
cleaved to form two subunits (A and B), linked
by a disulphide bond; wild-type codons 142
(Glu), 147(Val) and 148(Glu) have been deleted"
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  /*tag-
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               312...1910
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             Constion/Qualifices
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        Mekalanos
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 Mismatches
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               Score 18.2; DB 15;
Pred. No. 1.3e+02;
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    Length 1921;
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 Indels
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 0
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RESULT 10
AAQ54347/c
                                      a: 36333333333**
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Best Local Similarity
Matches 20, Conserv
                                              while their immunogenicity is not impaired. The specification includes the wild type DT coding sequence but does not include any moduli sequence. The wild type sequence was modified according to
                                                                                                           The resulting mateins are not toxic, making them useful in diphtheria vaccines. The risk of reversion to toxicity is much lower for the 147-148 double mutants than for the prior art 148 single mutant,
                                                                                                                                                                 uene (specifically the region encoding the DT-A fragment) results in deletion of the codons for Val-147 and active site residue Glu-148 and opt. deletion or substitution of other active residues
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          DI: protein exotoxin; NAD-dependent ADP-ribosyltransferase; vaccine; diphtheria toxoid; deletion mutant; mutein; variant; double mutant; reversion mutation; site-directed mutagenesis; ds.
Sequence 1936 BP; 574 A; 359 C; 470 G; 533 T; 0 other;
                                                                                                                                                                                                                                                             Claim 1: : 42pp: English.
                                                                                                                                                                                                                                                                                                                  New DNA encoding diphtheria toxin deletion mutants—wit toxicity and low risk of reversion, and derived loxuids
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   AAQ54337 standard; DNA; 1936
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               1862 GUGATCHACTGUTTTCTGGTACC 1840
                                      the description in the claims to give AAQ54337
                                                                                                                                                                                                                      Oligonucleotide-directed mutagenesis of the wild-type diphtheria
                                                                                                                                                                                                                                                                                                  transformed cells, useful in vaccines
                                                                                                                                                                                                                                                                                                                                                                            P PSDH; AAR44889
                                                                                                                                                                                                                                                                                                                                                                                              WPI: 1994-007178/01.
                                                                                                                                                                                                                                                                                                                                                                                                                                 Collier RJ, Killern K,
                                                                                                                                                                                                                                                                                                                                                                                                                                                                    (HARD ) HARVARD COLLEGE
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         18-JUN-1992;
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              17-MAY-1993;
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      W-0122210-W
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       Corynebacterium diphtheriae.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    Diphtheria toxin delta-147-148 mutant coding sequence.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       22-JUN-1994 (first entry)
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                AAQ54337
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            1 GTGCTCTANTCTTTTCTGGTACC 23
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 Concernative
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         9208-0901712
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              93WO-US04606
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           /product- delta:147:148_diphtheria_toxin
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 /*taq-
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      nocation/Qualifiers
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    70.0%;
87.0%;
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        Single state transfer
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 ۵
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     cleaved to form two subunits (A and B), Hi by a disulphide bond; wild-type endons 147
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     (Val) and 148(Glu) have been deleted"
                                                                                                                                                                                                                                                                                                                                                                                                                                   Mehalahos J;

    Mismatches

                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 Score 18.2; DH 15;
Pred. No. 1.3e(02)
n. Mismatches 3;
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   H
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            12 7 7 17 1
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   Cape
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            inked
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   S
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Matches Query Match

Local Similarity

70.0**%**;

Score 18.2; DB 15; Pred. No. 1.3e+02;

Length 1936; Indels

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Gaps

0;

Conservative

Ċ,

Mismatches

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RESULT 11
AAQ54339/c
ID AAQ543
                                                 글
                                                                                                         The resulting muteins are not toxic, making them useful in diphtheria vaccines. The risk of reversion to toxicity is much lower for the 147-148 double mutants than for the prior art 148 single mutant, while their immunogenicity is not impaired. The specification includes the wild-type or coding sequence but does not include any
                                                                                                                                                                                                                                                                       Claim 3;
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            W09325210-A
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     CDS
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             misc_difference 735..737
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               Corynebacterium diphtheriae
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       diphtheria toxoid; deletion mutant; mutein, variant, double mutant,
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       Diphtheria toxin (delta-147-148; E142X) mutant coding sequence
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     AAQ54339 standard; DNA; 1936 BP
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     1865
                                                Sequence 1936 BP; 573 A; 359 C; 468 G; 533 T; 3 other;
                                                                                                                                                                                                                                    Oligonucleotide-directed mutagenesis of the wild-type diphtheria
                                                                                                                                                                                                                                                                                                                  New DNA encoding diphtheria toxin deletion mutants - with no toxicity and low risk of reversion, and derived toxoids and
                                                                                                                                                                                                                                                                                                                                                                                                                Collier RJ, Killeen K,
                                                                                                                                                                                                                                                                                                                                                                                                                                            (HARD ) HARVARD COLLEGE
                                                                                                                                                                                                                                                                                                                                                                                                                                                                             18-JUN-1992;
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             17-MAY-1993;
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            23-DEC-1993.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        22-JUN-1994
                                                                                                                                                                                    Glu-148 and opt. deletion or substitution of other active residues
                                                                                                                                                                                                      gene (specifically the region encoding the STA fragment) results in deletion of the eaders for Val 147 and active site residue
                                                                                                                                                                                                                                                                                                    transformed cells, useful in vaccines
                                                                                                                                                                                                                                                                                                                                                                     P-PSDB; AAR44891
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             reversion mutation; site-directed mutagenesis; ds.
                                                                               the description in the claims to give AAOS4339
                                                                                              mutant sequences; the wild-type sequence was modified according to
    Local Similarity
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                1 GTGCTCTAATCTTTTCTGGTACC 23
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         protein exotoxin, NAD dependent ADF ribosyltransferase;
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   GTGATCTACTGTTTTCTGGTACC 1843
                                                                                                                                                                                                                                                                                                                                                                                 1994-007178/01.
                                                                                                                                                                                                                                                                       ; 42pp; English.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                               92US-0901712
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             93WO-US04606
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  /note= "single chain translation product is readily
cleaved to form two subunits (λ and B), lin
by a disulphide bond; wild type codons 147
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  /note= "wild-type GAG (Glu) codon substd by codon
for any other amino acid"
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  /product= delta 147 148,E142X_diphtheria_toxin
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     /*tag=
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   311..1913
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  /*taq∸
 70.0%;
87.0%;
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        142(Glu) has been altered"
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       (Val) and 148(Glu) have been deleted and
                                                                                                                                                                                                                                                                                                                                                                                                                  Mekalanos J;
 Pred. No.
              Score 18.2; DB 15;
1.3e+02;
                Length 1936;
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           vaccine
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     inked
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Matches

20;

Conservative

0;

Mismatches

Indels

0,

Gaps

0

Sequence 1936 BP;

573 A;

357 C; 470 G; 533 T; 3 other;

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8
AAQ54341/c
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       RESULT 12
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 CDS
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   Diphtheria toxin (delta-147-148; H21X) mutant coding sequence.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 AAQ54341 standard; DNA; 1936
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             1865 GTGATCTACTGTTTTCTGGTACC 1843
                            mutant, while their immunespecialty is not impaired. The specification includes the wild-type DT coding sequence but does not include any mutant sequences; the wild-type sequence was modified according to the description in the claims to give AAO54341.
                                                                                                                                                                                               Gligonoclectide directed motagenesis of the wild-type diphtheria gaze results in detection of the codons for Val-147 and active site residue which is essential for the full toxic activity of wild type DT is deleted or altered to encode a toxic activity of wild type DT is deleted or altered to encode a
                                                                                                                                                                                                                                                                                         Claim 7; ; 42pp; English.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        misc_difference 372..374
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            Corynebacterium diphtheriae.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             DT, protein exotoxin, NAS dependent ASF-ribosyltransferase, vaccine; diphtheria toxoid; deletion mutant; mutein; variant; double mutant; reversion mutation; site-directed mutagenesis; ds.
                                                                                                    portion of DT. The resulting muteins are not toxic, making them useful in diphtheria vaccines. The risk of reversion to toxicity is much lower for the 147-148 double mutants than for the prior art 148 single
                                                                                                                                          different amino acid residue. The third residue can be in the fragment A (see AAQ54341-7) or in the fragment B (see AAQ54348-Q54350) portion of DT. The resulting muteins are not toxic, making them useful
                                                                                                                                                                                                                                                                                                                                                                                                                                                             Collier RJ, Killeen K,
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   18-JUN-1992;
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 W09325210-A
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                                                                                                                                                                                                                                                                                                                                transformed cells, useful in vaccines
                                                                                                                                                                                                                                                                                                                                             New DNA encoding diphtheria toxin deletion mutants - with no toxicity and low risk of reversion, and derived toxoids and
                                                                                                                                                                                                                                                                                                                                                                                                         P-PSDB; AAR44893
                                                                                                                                                                                                                                                                                                                                                                                                                         WPI; 1994-007178/01.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       17-MAY-1993;
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     93WO-US04606
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            /note- "wild-type CAC (His) codon is replaced by codon for any other amino acid or is absent"
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        Location/Qualifiers
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 "single chain translation product is readil
cleaved to form two subunits (A and B), li
by a disulphide bond; wild type codons 147
(Val) and 148(Glu) have been deleted and
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       a
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 the His(21) codon is altered or deleted*
                                                                                                                                                                                                                                                                                                                                                                                                                                                             Mekalanos J;
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AAQ54342/c
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            Query Match
Best Local Similarity
             portion of DT. The resulting mateins are not toxic, making them useful in diphtheria "archaeta" is The rule) of reversion to the 147 148 double matants than for the prior art 148 single mutant, while their immunogenicity is not impaired. The specification
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              SCIC
                                                                             different amino acid residue. The third residue can be in the fragment A (see AAQ54341.7) or in the fragment B (see AAQ54348-Q54350)
                                                                                                           residue Glu 148; opt. a third residue which is essential for the full toxic activity of wild type DE is deleted or altered to encode a
                                                                                                                                         oligonucleotide-directed mutagenesis of the wild-type diphtheria gene results in deletion of the codons for Val-147 and active site
                                                                                                                                                                                                                                        New DNA encoding diphtheria toxin deletion mutants - with no toxicity and low risk of recention, and derived toxids and
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        Corynobacterium diphtheriae.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    DF; protein exetexin; NAD dependent ADP ribosyltransferase; vaccine, diphtheria toxoid; deletion mutant; mutein; variant; double mutant;
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   AAU54342 standard; DNA; 1936
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includes the wild type DT coding sequence but does not include any
                                                                                                                                                                                          Claim 7; ; 42pp; English
                                                                                                                                                                                                                            transformed cells, useful in
                                                                                                                                                                                                                                                                                                                                                                       (HARD ) HARVARD COLLEGE
                                                                                                                                                                                                                                                                                                                                                                                                       18 JUN 1992;
                                                                                                                                                                                                                                                                                                                                                                                                                                      17 MAY : 1993;
                                                                                                                                                                                                                                                                                                                                                                                                                                                                      54 DEC 1993.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      W09325210 A
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        reversion mutation; site directed mutagenesis,
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   Diphtheria toxin (delta-147:148; G22X) mutant coding sequence
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   AAQ54342;
                                                                                                                                                                                                                                                                                            P PSDB; AAR44894
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             | GTGCTCTAATCLILLE_GGAACC 23
                                                                                                                                                                                                                                                                                                           1994 007178/01.
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                                                                                                                                                                                                                                                                                                                                         Killeen K.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    (lirst estry)
                                                                                                                                                                                                                                                                                                                                                                                                      9208 0901712
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                /product
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87.0%;
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          "wild type ord (Cly) make is replaced by codon for any other amino acid or is absent N.B. the amino acid at position 22 of the wild-type of is given as Glu in the claims."
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             "single chain translation product is readily cleaved to form two subunits (A and H), limity a disulphide bond; wild type codons 147 (Val) and 148(Gln) have been deleted and the Gly(22) codon is altered or deleted."
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Pred. No. 1.30:02;
                                                                                                                                                                                                                              vaccines
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              Matches
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  HOST
                                                                                                                                                                                                                                                           WPI;
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    CDS
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            1865 GEGATCHACHGEFFFTCEGGTACC 1843
                                                                Oligonoclectide directed matagenesis of the wild type diphthoria gene results in deletion of the codons for Val-147 and active site residue Glo 148, opt. a third residue which is essential for the full toxic activity of wild type DT is deleted or altered to encode a
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             matant sequences, the Wild type Sequence was modified according to the description in the claims to give AAQS4342.
                different amino acid residue. The third residue can be in the tragment A (see AAQ54341-7) or in the tragment B (see AAQ54348-Q54350) portion of DT. The resulting muterns are not toxic, making them useful
                                                                                                                                                                                       transformed cells, useful in vaccines
                                                                                                                                                                                                                                                                                                             Collier RJ, Killeen K,
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       Diphtheria toxin (delta-147-148; K39X) mutant coding sequence
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          AAQ54343 standard; DNA; 1936
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              Sequence 1936 BP; 574 A; 359 C; 467 G; 534 T; 3 other;
                                                                                                                                                       Claim 7;
                                                                                                                                                                                                                         New DNA encoding diphtheria toxin deletion mutants - with no
                                                                                                                                                                                                                                                                                                                                                                              18-JUN-1992;
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                W09325210-A
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     Corynebacteriam diphtheriae
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     reversion mutation; site directed mutagenesis, ds.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     D); protein exotoxin; NAD-dependent ADP-ribosyltransferase;
diphtheria toxoid; deletion matant; mutein; mariant; double
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          AAQ54343;
in diphtheria vaccines. The risk of reversion to toxicity is much
                                                                                                                                                                                                         toxicity and low risk of reversion, and derived toxoids
                                                                                                                                                                                                                                                                                                                                           (HARD ) HARVARD COLLEGE
                                                                                                                                                                                                                                                                                                                                                                                                               17 · MAY - 1993;
                                                                                                                                                                                                                                                                                                                                                                                                                                                23-DEC-1993
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                                                                                                                                                                                                                                                            7806, AAR44895
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                                                                                                                                                                                                                                                                           1994-007178/01.
                                                                                                                                                       ; 42pp; English.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              Conservative
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                                                                                                                                                                                                                                                                                                                                                                                                                93WO-US04606
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     Location/Qualifiers
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               /product- diphtheria_toxin_mutant
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               finite. "single chain translation product is readily
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   /*tag=
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            70.0%;
87.0%;
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               cleaved to form two subunits (A and B), lip
by a disulphide bond; wild type codons 147
(Val) and 148(Glu) have been detected and
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 the Lys(39) codon is altered or deleted.
                                                                                                                                                                                                                                                                                                             Mekalanes
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   variant; double mutant;
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            Length 1936;
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 is absent"
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RESULT 15
AAQ54344/c
ID AAQ543
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Best Loca! :
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 lower for the 147-148 double mutants than for the prior art 148 single mutant, while their immunogenicity is not impaired. The specification includes the wild type or coding sequence but does not include any mutant sequences, the wild type sequence was modified according to the description in the claims to give AAQ54343.
different amino acid residue. The third residue can be in the
          Oligonucleotide-directed mutagenesis of the wild-type diphtheria gene results in deletion of the codons for Val-147 and active site residue Glu-148; opt. a third residue which is essential for the full loxic activity of wild-type DT is deleted or altered to encode a site of the full control of wild-type DT is deleted or altered to encode a
                                                                                           Claim 7; ; 42pp; English.
                                                                                                                         New DNA encoding diphtheria toxin deletion mutants - with no toxicity and low risk of reversion, and derived toxoids and transformed cells, useful in vaccines
                                                                                                                                                                                         P-PSDB;
                                                                                                                                                                                                                                         Collier RJ, Killeen K,
                                                                                                                                                                                                                                                                                                       18-JUN-1992;
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         Corynebacterium diphtheriae.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   DF; protein exotoxin; NAD-dependent ADP-ribosyltransferase; vaccine diphtheria toxoid; deletion mutant, mutein; variant; double mutant;
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     Diphtheria toxin (delta-147-148; G52X) mutant coding sequence
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  AAQ54344 standard; DNA; 1936 BP
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        Sequence 1936 BP; 571 A; 359 C; 470 G; 533 T; 3 other;
                                                                                                                                                                                                                                                                     (HARD ) HARVARD COLLEGE.
                                                                                                                                                                                                                                                                                                                                                                    23-DEC-1993.
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                                                                                                                                                                                                      1994-007178/01.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            20;
                                                                                                                                                                                          AAR44896
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           Similarity
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           Conservative
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                                                                                                                                                                                                                                                                                                     92US-0901712
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                                                                                                                                                                                                                                                                                                                                                                                                                                            /note- "single chain translation product is readily cleaved to form two subunits (A and B), lind by a disulphide bond; will-type codons 147 (Val) and 148(Glu) have been deleted and
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           /*tag-_b
/product=_diphtheria_toxin_mutant
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       /noté- "wild-type GGG (Gly) codon is replaced by codon for any other amino acid or is absent"
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        70.0%; Score 18.2;
87.0%; Fred: No. 1.
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                                                                                                                                                                                                                                                                                                                                                                                                                               the Gly(52) codon is altered or deleted"
                                                                                                                                                                                                                                       Mekalanes J;
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           0; Mismatches
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          .36:62
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       ры 15; Length 1936;
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            œ.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            Indels
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   vaccine;
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           0,
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         Caps
                                                                                                                                                                                                                                                                                                                                                                                                                                                                             inked
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           0;
```

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*83888838
á
                                           Matches
                                                                                   Query Match
                                                                                                                                                                                       fragment A (see AAQ54341-7) or in the fragment B (see AAQ54348-054350) portion of DT. The resulting mutains are not toxic, making them useful in diphtherar vaccines. The risk of reversion to toxicity is much lower for the 147-148 double mutants than for the prior art 148 single mutant, while their immunogenicity is not impaired. The specification includes the wild-type DT coding sequence but does not include any mutant sequences; the wild-type sequence was modified according to
                                                                                                                            Sequence 1536 BF, 574 A, 359 C, 467 G, 533 T, 3 other;
                                                               Local
  1 GTGCTCTAATCTTTTCTGGTACC 23
                                                                                                                                                                     description in the claims to give AAQ54344.
                                                             70.0%;
Similarity 87.0%;
                                           Conservative
                                        0;
                                                                               Score 18.2; DB 15;
                                                               Pred.
                                        Mismatches
                                                               NO.
                                                               1.3e+02;
                                                                                 Length 1936;
                                        Indels
                                        0;
```

В

1865 GTGATCTACTGTTTTCTGGTACC 1843

0

Search completed: January 14, Job time: 7.29613 sees

2003, 11:52:35

